

# Evidence-Based Treatment of Gastroesophageal Reflux in Neonates

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## LEARNING OBJECTIVES

After reading this article, the reader will be able to:

- Identify predisposing factors for GER in neonates.
- Recognize non evidence-based interventions for GER in neonates.
- Identify evidence-based interventions for GER in neonates.
- Understand the relationship between GER and apnea.

Preterm infants are at risk for many health problems including gastroesophageal reflux (GER), which is very distressing to parents and caregivers. Infants with GER experience symptoms such as regurgitation, crying, irritability and arching within 30 minutes of feeding. The purpose of this article is to examine GER in neonates and review research evidence to support effective interventions. Common interventions such as elevating the head of the bed, holding the infant upright, using prone or left-lateral positioning, thickening feedings and use of medications will all be discussed. In addition, research evidence about the supposed relationship of GER to apnea in preterm infants will be presented.

## “Show Me the Evidence”

It is estimated that only 85% of healthcare practice has been scientifically validated.<sup>1</sup> Ideas become habits, and these habits become established practice, without any research to support them. Several neonatal nursing texts recommend interventions for neonatal GER such as elevating the head of the bed, holding the infant upright after feeds,<sup>3</sup> and prone positioning with the head of the bed elevated, without sufficient supporting evidence.<sup>1-4</sup> For example, many caregivers in neonatal intensive care units (NICUs) position infants with the head of the bed elevated, an anecdotal remedy, upon the recommendations of outdated reference books that offer conflicting advice, or they place the infant in a prone position despite the recommendation of the American Academy of Pediatrics against the practice after 37 weeks.<sup>5</sup>

Of the various methods to evaluate research, the most accepted is to classify a study by how it was performed (study method), the number of subjects studied, and whether the results can be reproduced by others. Many professionals believe this model does not allow for the incorporation of clinical expertise. However, history has shown that numerous examples of health-care interventions that seem to work and benefit individuals, are actually found to have no benefit and/or to be harmful in randomized controlled trials (RCTs).<sup>6</sup> Some examples of non-evidence-based practice in neonatal care are unrestricted oxygen use, resulting in retinopathy; restriction of oxygen use, resulting in CNS damage or death; postnatal steroids and resuscitation with 100% oxygen.<sup>7</sup> In contrast, surfactant therapy in preterms is an example of a well-studied, evidence-based intervention.<sup>7</sup>

While the majority of daily nursing decisions do not emerge from RCTs, best practice encourages professionals to thoughtfully examine the literature in order to validate new practices and re-evaluate established ones.<sup>8</sup> Some authors have taken the different classifications of research and created a pyramid that puts more reliable evidence near the top and more opinionated evidence near the bottom. The pyramid model takes evidence and weighs it based upon established criteria:<sup>8</sup>

- A. Level I: systematic reviews from RCTs, or clinical guidelines based on systematic reviews of RCTs.
- B. Level II: evidence from a single, well-designed RCT.
- C. Level III: evidence from a well-designed study without randomization.
- D. Level IV: evidence from case-controlled and cohort studies.
- E. Level V: evidence from the opinion of an established authority or committee.

Using this type of classification helps determine the reliability and validity of a study, and allows one to apply the information to clinical practice.

An extensive literature search for studies that discussed GER and positioning was undertaken and reviewed. The databases searched were the Cumulative Index

to Nursing and Allied Health Literature (CINHAL), the Cochrane library, Medline, PubMed and Google Scholar. As the articles were read, cited articles were noted and retrieved. Keywords were: gastric esophageal reflux, gastric-esophageal reflex, head of bed elevation, positioning, neonate, infant and baby. Eight articles, including one Cochrane review, were chosen to review and critique for this analysis.

### Definitions and Incidence

After ingestion, food passes through the esophagus into the stomach via the lower esophageal sphincter, which opens and allows the food to enter the stomach. The sphincter then closes to prevent reflux of food and stomach acid back into the esophagus.<sup>9</sup> Factors predisposing infants to GER include gastric emptying time,<sup>9a</sup> all feeding as liquid, and positioning after feeding. In late preterm infants the mean time to half emptying of the stomach varied from 34.9 to 75.3 minutes depending on positioning.<sup>10</sup> Enterally-fed infants take up to 180 milliliters per kilogram per day, a volume comparable to an adult ingestion of about 14 liters of fluid per day.<sup>11</sup> Additionally, as soon as the infant completes the feeding he or she is often laid down to sleep. Some 67% of normal 4-month-old infants regurgitate at least one time per day.<sup>12</sup>

GER is a developmental condition of young infants and older adults. In neonates the reflux of stomach contents into the mouth (spit up) is quite common and usually not accompanied by any evidence of distress. GER of this degree typically decreases with age and is uncommon by about 10 months of age. If reflux into the esophagus or mouth is accompanied by distress, the infant may be said to have gastroesophageal reflux disease (GERD). Symptoms of GERD include: regurgitation, irritability, excessive crying, disturbed sleep, impaired feeding tolerance, poor weight gain and respiratory complications. GERD that is more than minimally symptomatic may require more extensive diagnosis and treatment.<sup>14</sup>

There is a widespread belief that GER either causes or exacerbates apneic episodes in preterm infants. Apnea, a cessation of

respirations for more than 20 seconds, is common in preterm infants and may be either primary (apnea of prematurity) or secondary, due to other causes such as position, temperature, sepsis etc. Most apneic episodes are central (inspiratory efforts are absent) or mixed (airway obstruction with central apnea) and do occur frequently in premature infants. The younger the gestational age, the greater the frequency of apneic episodes.<sup>15</sup>

However, both an RCT and a pH-probe study of 102 infants could establish no relationship between GER and apnea.<sup>16,17</sup> In the RCT, researchers concluded that GER does not cause, prolong or exacerbate apnea.<sup>16</sup> Apnea of prematurity usually resolves as the infant reaches 40 weeks corrected gestational age, whereas GER symptoms often are seen in infants up to age 10 to 12 months.<sup>12</sup> Caregivers who understand the physiology, pathophysiology and timing of each condition can avoid causal conclusions when data do not support a relationship.

Knowledgeable caregivers are also able to provide interventions for each condition, independent of the other.

### Interventions for GER

When an infant has symptoms of GER, caregivers and parents will attempt a number of approaches to alleviate the infant's distress. Following are commonly used interventions and the research evidence for each.

#### *Elevating the Head of the Bed*

Because of anecdotal practice and unit history, head-of-the-bed elevation is the first treatment used for many infants with symptoms of GER. This treatment is suggested in many nursing texts and articles but has not been validated. Some texts cite a 2002 review of the literature that discusses the problem of GER in neonates; however, the author of the review notes that the information and recommendations for neonates are an extrapolation of research performed on older infants.<sup>2</sup> This article cites factors that may contribute to GER: (1) increased intra-abdominal pressure; (2) excessive crying; (3) delayed gastric emptying and (4) sluggish esophageal motility. The researcher also notes that supine, right lateral and elevated positioning in a

car seat exacerbate the symptoms of GER. Although prone positioning with 30 degree elevation, and left lateral positioning lessen the symptoms of GER, the author points out that the prone position is associated with SIDS and is therefore not recommended.<sup>2</sup> The articles referenced in the review are the same as those used for this critique and do not list any studies that support head of the bed elevation.<sup>2</sup>

Two articles in 1983 evaluated positioning for the relief of GER in infants.<sup>19,20</sup> Placing an infant upright in a car seat at a 60 degree angle had been used to treat GER — without evidence to support the practice. When studied, using a car seat did not decrease, but rather increased, GER symptoms because the lower esophageal sphincter is more likely to be submerged in the 60 degree head-elevated position.<sup>20</sup> In two prospective controlled comparisons, one of 9, the other of 15 infants with GER symptoms, each infant had a pH probe and continuous pH monitoring for 24 hours while positioned in either a car seat or prone, with head of the bed elevated. The studies monitored the percentage of time with esophageal pH below 4, number of episodes when pH was less than 4, the number of low pH episodes lasting longer than 5 minutes and the duration of the longest episode. Both studies showed that infants in car seats had longer exposure to GER, for a longer period of time, and had more episodes.<sup>19,20</sup> These studies did not look at either of the positions compared to any other sleeping position

In 1990, another study by the same researchers compared the efficacy of 30 degree head-of-the-bed elevation to prone positioning in 100 infants younger than six months of age, 90 of whom had suspected GER. Using pH probes, the researchers monitored esophageal pH continuously for 24 hours. Recordings were assessed for number of minutes with a pH less than 4, mean duration of each episode, number of episodes with pH less than 4, and number of episodes of less than 5 minutes duration.<sup>21</sup> Each infant was randomly placed in one position and then, half way through the study, changed to the other position. The results revealed “no measure of reflux that was significantly better in

the head-elevated position than in the prone position.”<sup>21</sup> The study concluded that positioning infants in head-elevated positions was not worth the effort. Although the first study in 1983 showed head-of-bed elevation of 30 degrees was superior to car seat sitting at 60 degrees, the 1990 study showed that head-of-bed elevation of 30 degrees was, in fact, not superior to the prone position for the relief of GER symptoms.<sup>19,21</sup>

Elevation of the head of the bed came from the supposition that infants lying flat may be more susceptible to GER symptoms.<sup>20</sup> Caregivers have elevated the head of the bed with wedges and created cloth slings to hold the infant in place once the head is elevated. Some crib companies now manufacture and sell cribs that allow the head of the bed to be elevated. Advice and recommendations for parents are readily available on multiple internet sites. Some of these interventions seem benign, but may increase the length of hospital stay and be costly to parents. Parents may be encouraged to buy a special crib, wedges and/or slings for an existing crib at home. Worse, the interventions can lead to unsafe sleeping conditions for the infant. For example, the use of pillows or blankets contributes to an increased risk of suffocation. Elevation of the head of a normal crib may make the infant vulnerable to a fall.

#### ***Left Lateral Position***

In 1997, 24 infants with symptoms of GER were randomly assigned to one of four positioning groups: prone, supine, right lateral or left lateral. In addition, there was a comparison of infants placed horizontally to those positioned with the head of the bed elevated 20 degrees.<sup>22</sup> After 24 hours, infants were randomly assigned to another group. All infants had a pH probe to monitor acid levels in the esophagus. Reflux index (i.e., percent of time with a pH less than 4), number of episodes with a pH less than 4 during 24 hours, number of episodes lasting more than 5 minutes, and the duration of the longest episode were monitored. Table 1 shows the reflux index in various study positions. There was a significant difference between right lateral position and supine position compared to left lateral and prone

position. There was no significant difference between horizontal and head-of-bed elevation. Therefore, these researchers concluded that “in this study no benefit for head elevation was noted.”<sup>22</sup>

In 1999 another investigation using the reflux index reproduced the same results in a sample of 18 infants in a NICU.<sup>18</sup> Left lateral, right lateral and prone positions were investigated with 24 hour pH probes. The number and severity of reflux episodes for infants in the right lateral position exceeded those of the infants in the left lateral and prone positions. Because the least frequent and least severe symptoms occurred in infants placed in the prone or left lateral position, the study concluded that the left lateral position be adapted as a position for infants with symptoms of GER.<sup>18</sup>

In 2009, a Cochrane Review analyzed five different studies regarding head-of-bed elevation.<sup>12</sup> A 1999 study by Bagucka found that the head-elevated position was not helpful in decreasing GER.<sup>23</sup> Other research covered in the Cochrane Review includes the previously listed articles by Tobin and Orenstein.<sup>19,22</sup> The Cochrane Review authors classified the quality of the analyzed studies as good. Each study used pH probe monitoring for 24 hours

**Table 1: Reflux Index Related to Infant Position**

<b>Infant Position</b>	<b>Reflux Index*</b>
Supine	15.3
Right Lateral	12.0
Left Lateral	7.7
Prone	6.7
Horizontal	10.7
Elevated Head of Bed	10.1
*Normal average index is 10 for infants <12 months of age	

as a determination of severity of symptoms. Some research compared infants with head-of-bed elevated to those positioned in an elevated car seat, some compared infants placed prone to those placed supine; some compared left lateral to right lateral positioning.<sup>19,20</sup> Of the five different investigations reviewed, none found any significant decrease in GER symptoms for infants with head-of-bed elevation. Elevated pH in the esophagus was the same for infants positioned flat as with the head of bed elevated.<sup>19-23</sup> Prone and left lateral positioning was significantly superior to supine or right lateral positioning. In fact, research that

analyzed positioning greater than 30 degrees (i.e., in car seat or using positioning aids) found that prone and left lateral positioning were superior to elevation. Due to the risk of sudden infant death syndrome (SIDS), the prone position is not recommended by the study authors or the review authors. It should be noted that the studies evaluated in the Cochrane Review were of small sample size and, due to the nature of the research, blind randomization was not achieved.

In 2007, a randomized controlled trial of 22 preterm infants with GER symptoms assessed whether left side lying position was effective in

decreasing non-acid GER, as well as acid GER. The infants were monitored by pH probes for 24 hours to assess the number and length of GER occurrences.<sup>24</sup> Liquid versus air reflux was differentiated in the study using modern impedance equipment. Each patient was randomly positioned in right lateral, left lateral, prone and supine positions. Findings were similar to previous studies showing the least GER occurrences in prone position, the next fewest in the left lateral position, then right lateral, with the most occurrences in the supine position. Results were the same for liquid reflux and air reflux. The authors concluded

that there was no statistical difference between prone and left lateral positions because only 1.9 episodes occurred in left lateral position and 1.1 episodes in prone position. The authors also stated that the “findings do not provide any information on clinical improvement” but rather a “simple way to limit GER.”<sup>24</sup>

Therefore, this review of the literature shows that head-of-bed elevation is not supported by research. The recommended positions for infants who are experiencing symptoms of GER are either prone or left lateral side lying.

### Other Interventions for GER

More invasive interventions, such as thickening feeds and medication, have been used for GER. Evidence does not support the safety or efficacy of these modalities. Caregivers have postulated that thickened feedings alter stomach contents from fluid to a more solid consistency, decreasing the occurrence of regurgitation into the esophagus. But no reduction of GER has been noted from thickening breast milk with a starch additive. Moreover, a possible relationship between thickened feedings and necrotizing enterocolitis was noted.<sup>24a</sup> In term infants fed formula however, there is some evidence that thickened formula can reduce the number of regurgitation episodes.<sup>24b</sup>

There is widespread use of anti-reflux medications to treat GER in neonates—with a lack of efficacy noted in clinical studies.<sup>25</sup> Off-label use (without approval by the Food and Drug Administration for use in neonates) of metoclopramide and ranitidine is so common that they are ranked first and fourth, respectively, among medications most frequently used in the NICU.<sup>25</sup> Adverse effects of these medications in preterms include an increased risk of hospital-acquired sepsis and a higher incidence of necrotizing enterocolitis. Although clinical studies demonstrate no statistical benefit in the reduction of GER symptoms from medications and/or thickening of breast milk, these interventions continue to be prescribed in NICUs.

### Implications and Recommendations

Based on the research reviewed here, infants with symptoms of GER should be placed flat to sleep in a prone position or left lateral position

until they are 37 weeks corrected gestational age, after which the prone position should be avoided. Elevating the head of the bed, thickening feedings, and use of medications have not been shown to be effective in decreasing the duration or severity of GER symptoms.

When an infant presents with symptoms of GER, “a stepwise approach, based mainly on conservative interventions is the best therapeutic choice.”<sup>24</sup> Other causes for the symptoms should be eliminated with a thorough review of perinatal history and a physical assessment. While considering differential diagnoses, interventions to diminish symptoms of GER can be initiated. Holding the infant upright after feedings helps eliminate air from the stomach with burping. Holding the infant for 30 minutes after feeding, the usual time when acid reflux occurs, diminishes symptoms, enables the caregiver to comfort the infant, and helps transition to a sleep state. Placing the sleeping infant in a left lateral position for at least 30 minutes and then repositioning onto the back for sleep, relieves symptoms and complies with AAP “Back to Sleep” guidelines. More research is required to give long-term recommendations.

### Conclusion

An evaluation of the literature has shown that some of the most often applied positional interventions: head of bed elevation, slings and wedges, do not have evidence-based origins and do not stand up to physiological testing. Preconceived ideas withhold the relief that could be available by recommended interventions, such as horizontal prone and horizontal left lateral positions. This critical review of the literature shows the efficacy of the prone and left-lateral positions and reveals the need for evidence-based practice.

### ABOUT THE AUTHOR

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